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Title

METHOD OF PRODUCTION OF AN ISOMALTULOSE-CONTAINING ENTERAL NUTRIENT

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METHOD OF PRODUCTION OF AN ISOMALTULOSE-CONTAINING ENTERAL NUTRIENT

FIELD OF THE INVENTION

[0001] The present invention relates to a method of production and use of an enteral nutrient, in particular an enteral solution or suspension.

BACKGROUND OF THE INVENTION

[0002] An enteral nutrient is a nutrient which is supplied either orally or gastrointestinally to a patient or consumer without decomposition of the nutrient taking place in the user's mouth or pharynx. Because of this, enteral nutrients are as a rule in the form of solutions or suspensions, and are used in both humans and animals. Complete enteral nutrients usually contain fat, carbohydrate and protein components and frequently also additives, for example, for increasing their stability or improving flavor. Their production as a rule includes pasteurization, homogenization, and sterilization steps using high temperatures and pressures.

BRIEF SUMMARY OF THE INVENTION

[0003] A complete enteral nutrient is known from US Patent 4,497,800. The enteral solution described there has a low pH value and consequently is microbially quite stable. However, the very high osmolality, and the necessity of adding emulsifiers, are a disadvantage.

[0004] A further enteral nutrient is known from EP 0 126 666, but nevertheless is characterized by a bitter taste.

[0005] From US Patent 4,959,350, a liquid enteral nutrient is known, likewise with a low pH value, and distinguished by an improved taste. To obtain microbial stability, the solution was pasteurized at 85°C for 4 seconds.

[0006] Common to the above-mentioned nutrients is that these are open to improvement from the nutrition physiological standpoint. Thus as a rule they contain glycemic carbohydrates which lead to a rapid and high blood glucose level and have a high insulin requirement which burdens the metabolism. Alternative carbohydrates such as fructose, on the other hand, supply no nutrition-physiologically useful glucose and decompose during the production of the nutrient solutions. In addition, the known methods for the production of enteral solutions frequently lead to decomposition of components, particularly ketoses, present in the enteral nutrient, due to the process conditions used for pasteurization and sterilization. The patient consequently receives on the one hand too little of the components concerned, particularly ketoses, and on the other hand too much of conversion products, for example, products of the Maillard reaction such as AGEs (Advanced Glycation End-products).

DETAILED DESCRIPTION OF THE INVENTION

[0007] The present invention is therefore based on the technical problem of providing a method for the production of an enteral nutrient, particularly ketose-containing enteral solution or suspension, which overcomes the said disadvantages and in particular leads to a technically simple and inexpensive preparation of a germ-free or germ-reduced enteral nutrient which is particularly valuable from the nutrition physiological standpoint, is low glycemic, and nevertheless provides glucose.

[0008] The present invention overcomes the technical problem on which it is based by the provision of a method for the production of an isomaltulose-containing enteral nutrient, in particular an enteral solution or suspension, comprising the steps of (a) provision of the starting components: water, fat, at

least one nitrogen-containing component, and at least one carbohydrate-containing component, particularly isomaltulose, (b) subsequent homogenization of the starting components provided, and (c) subsequent pasteurization of the starting components for 10-30 seconds at temperatures ≥135°C, preferably 135-137°C. The order of steps (b) and (c) can of course be interchanged, that is, in such an embodiment the method relates to a method with the sequence (a) provision of the starting components, (c) pasteurization of the provided components under the said conditions, and (b) subsequent homogenization of the pasteurized starting components.

[0009] The present invention also overcomes the technical problem on which it is based by the provision of a method for the production of an isomaltulose-containing enteral nutrient, in particular an enteral solution or enteral suspension, comprising the steps of (a') provision of the starting components: water, fat, at least one nitrogen-containing component, and at least one carbohydrate-containing component, particularly isomaltulose, (b') subsequent homogenization of the starting components provided, and (c') subsequent sterilization, particularly autoclaving, of the starting components for 5-15 minutes at temperatures ≥120°C, preferably 125-128°C. The order of steps (b') and (c') can of course be interchanged, that is, in such an embodiment the method relates to a method with the sequence (a') provision of the starting components, (c') sterilization of the provided components under the said conditions, and (b') subsequent homogenization of the autoclaved starting components.

[0010] In a further embodiment, the invention relates to a method with the said steps (a), (b), and (c), or (a), (c), and (b), wherein in addition to the last method step of the said method, if necessary with the addition of additional materials, sterilization is performed, particularly autoclaving of the homogenized and pasteurized starting components, preferably autoclaving at temperatures ≥120°C, preferably 125-128°C, for a period of 5-15 minutes.

[0011] In a further preferred embodiment, it is provided that the said pasteurizing step and/or the said sterilization step are performed at a pH value of 6.5-8.0, preferably 6.5-7.5. In a preferred embodiment, it can be provided that the adjustment of the pH value takes place at the beginning of, or during, the said production method.

[0012] In connection with the present invention, "enteral nutrient" is in particular understood to mean a germ-reduced, substantially germ-free or low-germ, enteral solution or enteral suspension which is suitable for the peroral or gastrointestinal (probe feeding) nutrition of the human or animal body. "Germs" are microbial organisms, or reproductive products of such organisms, particularly fungi, spores, yeasts, bacteria, bacilli, protozoa, algae, lichens, cyano-bacteria, etc. In connection with the present invention, by "pasteurizing" is understood a killing brought about by heat of special kinds of germs and viruses, complete freedom from germs and viruses not being attained. By "sterilization", particularly autoclaving which is sterilization in a steam pressure vessel, is understood a process directed to the complete killing of germs and viruses, which in particular according to the invention uses heating to at least 120°C.

[0013] The invention thus envisages the provision of an enteral nutrient which contains isomaltulose (also termed palatinose) as the carbohydrate, besides the water, fat, and nitrogen-containing components required for complete nutrition. Isomaltulose provides nutrition-physiologically favorable glucose by slow liberation, without burdening the metabolism with high insulin requirement. Isomaltulose is thus found to be particularly advantageous for the enteral nutrient produced and used according to the invention because of its slow glucose liberation and its insulin-independent metabolism with full energy value. Furthermore, the production and use according to the invention are distinguished by a reduced content of AGEs. In a preferred embodiment of the present invention, no carbohydrate other than isomaltulose is present in the enteral nutrient, particularly no further sugar. Isomaltulose in this embodiment is the

one and only carbohydrate, particularly the only sugar, in the enteral nutrient. In a further preferred embodiment, it can however be provided that isomaltulose is present together with other carbohydrates, for example, glucose, fructose, invert sugar, lactose, maltose, trehalose, maltodextrin, pectin, saccharose, starches, hydrolyzed starches, or sugar conversion materials such as isomaltol or other sugar alcohols such as lycasin, mannitol, sorbitol, xylitol, erythritol, maltitol, lactitol, 1,6-GPS (6-O-α-D-glucopyranosyl-D-sorbitol), 1,1-GPM (1-O-α-D-glucopyranosyl-D-mannitol, or 1,1-GPS (1-O-α-D-glucopyranosyl-D-sorbitol), etc. In the last-named embodiment, it is particularly preferably provided according to the invention that the isomaltulose replaces a portion of the carbohydrate usually present in a commercially obtainable enteral nutrient, in particular, replaces ≥30, ≥40, ≥50, ≥60, ≥70, ≥80, ≥90, or ≥95 wt.-% (based on dry substance of all carbohydrates in the enteral nutrient).

[0014] The invention particularly provides for the use as the carbohydrate, isomaltulose alone or in substantial proportions in the enteral nutrient, and to pasteurize the isomaltulose-containing starting components for 10-30 seconds at temperatures of at least 135°C, particularly 135-137°C, and/or to sterilize the isomaltulose-containing starting components for 5-15 min. at temperatures of at least 120°C, particularly at 125-128°C. A reduction of carbohydrate decomposition can usually be attained by lower temperatures. It has surprisingly been found that a reduction of the ketose decomposition can be achieved, even at high temperatures, by reducing the residence time. By maintaining this recipe and pasteurizing conditions, a particularly high isomaltulose content in the homogenized, ready for use enteral nutrient is surprisingly obtained. The enteral nutrient obtained gently in this manner, nevertheless germ-free or germ-reduced, is distinguished in a particularly advantageous manner by high storage stability, high microbial stability, and good organoleptic properties, and has a pleasant, sweet taste. Furthermore, isomaltulose is split by the glucosidases of the small intestinal wall only in a delayed manner. In comparison with the rapidly digestible carbohydrates, this results in a slow rise of blood glucose. The released

fructose is simultaneously reabsorbed. Both together lead to isomaltulose requiring hardly any insulin for metabolism, differing from the rapidly digestible, highly glycemic foodstuffs. Moreover, isomaltulose is particularly suitable, because of the delayed decomposition in the small intestine, for maintaining oxidative metabolism. The present enteral nutrient is thus outstandingly suitable as a "slow release" nutrition, i.e., nutrition with delayed, continuous carbohydrate liberation, which at the same time is suitable, because of the low insulin requirement, for persons suffering from disturbances of blood glucose metabolism.

[0015] In a further preferred embodiment of the invention, as mentioned, following on the last step of the production method according to the invention, that is, after the pasteurizing or homogenizing step (b) or (c), a step of sterilizing the homogenized starting components is performed. As long as the obtained enteral solution is filled after pasteurizing into sterile containers, this sterilizing step can be dispensed with.

[0016] It can also be provided according to the invention to dry the product after pasteurizing, homogenizing, or sterilizing, particularly autoclaving, in particular to spray dry it and possibly to agglomerate it. The powder obtained is reconstituted before use by dissolving in water.

[0017] The invention therefore relates to the isomaltulose-containing enteral nutrients produced by means of the method described in the present technical teaching.

[0018] In a preferred embodiment of the invention, this relates to an enteral nutrient with 70-80 wt.-% water (based on the total weight of the whole solution or suspension).

[0019] In a further preferred embodiment of the present invention, this relates to an enteral nutrient with 1-3.5 wt.-% nitrogen-containing components (based on the total weight of the enteral nutrient).

[0020] In a further preferred embodiment of the present invention, this relates to an enteral nutrient with 2-4.5 wt.-% fat (based on the total weight of the enteral nutrient).

[0021] In a further preferred embodiment of the present invention, this relates to an enteral nutrient with 6-11 wt.-% carbohydrate (based on the total weight of the enteral nutrient). In a preferred embodiment, the isomaltulose content is 1-20 wt.-%, preferably 5-15 wt.-% (based on the total weight of the solution or suspension).

[0022] In a further preferred embodiment of the present invention, the enteral nutrient, in particular the enteral solution, has a pH value of 2-10, particularly 2-8, preferably 6.5-8.0, more preferably 6.5-7.5.

[0023] In a further preferred embodiment of the present invention, (in relation to the total energy content), the fat content, particularly triglycerides, is 3-60%, the content of nitrogen-containing components is 10-35%, and the carbohydrate content is 5-87%.

[0024] In a particularly preferred embodiment, the osmolality is equal to or less than 350 milliosmal.

[0025] In a particularly preferred embodiment of the present invention, the fat used is a vegetable fat, particularly a vegetable oil, for example, corn oil, coconut oil, soy oil or sunflower oil, or mixtures thereof. It is of course also possible to use other fat components, particularly synthetic oils.

[0026] In a further preferred embodiment, used as the nitrogen-containing component are proteins, peptides, amino acids, mixtures thereof, protein or peptide hydrolysates, particularly hydrolyzed lactalbumin, hydrolyzed milk, acid milk, casein, hydrolyzed casein, caseinates, hydrolyzed soy bean protein, and/or free amino acids. In a preferred embodiment, nitrogen-containing components are used which represent proteins of vegetable origin or are produced therefrom. According to the invention, there can for example be used

protein hydrolysates from colza, beans, wheat, sesame or peas. Mixtures of such hydrolysates can of course be used.

[0027] In a further preferred embodiment, it is provided that the starting components of step (a) also include flavorants, buffers, salts, preservatives, odorants, further sweeteners, minerals, vitamins, inert materials, acids compatible with foodstuffs, trace elements, electrolytes and/or emulsifiers, pharmacologically active materials, antibiotics, antioxidants, etc.

[0028] The invention also relates to the use of isomaltulose in enteral nutrients or for the production of enteral nutrients, preferably produced according to one of the abovementioned methods, as a low-glycemic carbohydrate, that is, with low insulin requirement, the enteral nutrient being suitable for healthy human or animal bodies or for human or animal bodies with disturbed glucose and/or insulin metabolism.

[0029] Further advantageous embodiments of the present invention will become apparent from the dependent claims.

[0030] The invention will be described in detail using the following examples.

Example 1
Production and Pasteurizing an Enteral Solution with Palatinose Addition (by UHT (Ultra High Temperature))

[0031] (A) The solution components according to the following recipe (Section B) are taken up in water in a glass beaker in the sequence salts, vitamins, carbohydrates and finally proteins and are homogenized using an ultra Turrax stirrer. The homogenized mass is then forwarded through the trial plant by means of a pump. The trial plant consists of the sections inlet, preheater, UHT heater, heat retainer, cooler and outlet. The UHT heater is indirectly heated

with steam, as usually used for the UHT heating of milk. The residence time in the heat retainer system is varied by means of the pump delivery. The pasteurization according to the invention is performed according to the trial times and temperatures given in the following Table 1.

[0032] The analytical data of the carbohydrate components are obtained by high performance anion exchange chromatography (HPAEC) with NaOH as eluent and amperometric detection.

Table 1

			Batch 1	Batch 2	Batch 3
T	**(Temperature)**	**[°C]**	130	135	140
T	**(time)**	**[sec.]**	50 (control)	30	10
Isomaltulose [g/kg]					
	Solution before UHT step		101.07	100.23	100.07
	Solution after UHT step		69.25	72.52	81.20
Isomaltulose decomposition [%]			31	28	19

[0033] The germ and virus numbers obtained were substantially identical in all three trials. However, the isomaltulose decomposition was markedly reduced in the method according to the invention (Batches 2 and 3) in contrast to a control batch with reduced temperature and longer pasteurizing time. A reduction of decomposition by about a third resulted from the shortening of the incubation times.

(B) Example of Recipe with Isomaltulose

Raw Material	Kg/100 kg
Water	76.379001
Isomaltulose	10.000000
Glucidex 12 maltodextrin 10 DE	5.295000
Calcium caseinate, spray dried	3.400000
Fat mixture, standard	3.110000
Sodium caseinate, spray-dried	0.900000
Potassium chloride	0.185500
Emulsifier, Myverol 18-0, as monoglyceride	0.125000
Tripotassium citrate monohydrate	0.110000
Potassium dihydrogen phosphate, K11-01	0.105000
Emulsifier, Halocithin 02-F	0.080000
Trisodium citrate dehydrate, grade 6090	0.080000
Tricalcium phosphate	0.060000
Glucidex 21 Maltodextrin 20 DE	0.044122
Magnesium oxide, heavy	0.040000
Potassium dihydrocitrate, anhydrous	0.030000
Choline bitartrate, coated	0.022000
Vitamin C, pulverized	0.013600
Iron-II lactate	0.005000
Zinc sulfate monohydrate	0.002750
Sodium chloride	0.002000
Nicotinamide	0.002000
Antioxidant, ascorbyl palmitate	0.001500
Vitamin A acetate 325	0.001400
Potassium iodide, 1% I trituration	0.001150
Cu-II gluconate	0.000845
Mn-II sulfate monohydrate	0.000715
Ca D-pantothenate	0.000550
Sodium molybdate, 1% molybdenum trituration	0.000500
Vitamin D3	0.000450
Sodium fluoride	0.000400
Sodium selenide 1% selenium trituration	0.000300
Vitamin B12 0.1%	0.000240
Chromium-III chloride, 1% chromium trituration	0.000225
Vitamin B6 HCl	0.000225
Vitamin B2	0.000187
Vitamin B1 HCl	0.000150
Vitamin K1 5% SD	0.000060
Folic acid	0.000024
Biotin, d	0.000006
Total	100.000000

Example 2

Sterilization by Autoclaving

[0034] The solution components according to the recipe of Example 1 (Section B) are received in water in a glass beaker in the sequence salts, vitamins, carbohydrates and finally proteins and were homogenized by means of an ultra Turrax stirrer. The homogenized mass is then transferred to an autoclave and sterilized in a laboratory steam autoclave. According to this description, the autoclaving (sterilization) according to the invention is performed with the trial times and temperatures as given in the following Table 2.

[0035] The analytical data for the carbohydrate constituents were obtained by high performance anion exchange chromatography (HPAEC) with NaOH as the eluent and amperometric detection.

Table 2

Results:

	Batch 1	Batch 2	Batch 3
T (Temperature) [°C]	115	121	128
T (time) [sec.]	30	15	5
P (bar_{abs})	1.7 (control)	2.1	2.5
Isomaltulose [g/kg]			
Solution before autoclaving	100.25	100.13	100.26
Solution after autoclaving	58.71	61.27	69.37
Isomaltulose decomposition [%]	41	39	31

[0036] The germ and virus numbers obtained were substantially identical in all three trials. However, the isomaltulose decomposition was markedly reduced in the method according to the invention (Batches 2 and 3) in contrast to a control batch with reduced temperature and longer sterilization time. A reduction of decomposition by about 33% resulted from the shortening of the incubation times.

Example 3

Production, Pasteurizing (UHT Heating) and Sterilizing (Autoclaving) of an Enteral Solution with Palatinose Addition

[0037] The solution components according to the recipe of Example 1 (Section B) are taken up in water in a glass beaker in the sequence salts, vitamins, carbohydrates and finally proteins and are homogenized using an ultra Turrax stirrer. The homogenized mass is then forwarded through the trial plant by means of a pump. The trial plant consists of the sections inlet, preheater, UHT heater, heat retainer, cooler and outlet. The UHT heater is indirectly heated with steam, as usually used for the UHT heating of milk. The residence time in the heat retainer system is varied by means of the pump delivery. The pasteurization according to the invention is performed according to the trial times and temperatures given in the following Table 3.

[0038] The analytical data of the carbohydrate components were obtained by high performance anion exchange chromatography (HPAEC) with NaOH as eluent and amperometric detection.

Table 3

Results:

	Batch 1	Batch 2	Batch 3
T (Temperature) [°C]	130	135	140
T (time) [sec.]	50 (Control)	30	10
Isomaltulose [g/kg]			
Solution before UHT step	100.65	99.38	100.05
Solution after UHT step	66.38	76.36	83.72
Isomaltulose decomposition [%]	34	23	16

[0039] The product of reaction batch 3 (i.e., the product with the highest residual isomaltulose fraction after the pasteurizing step) is transferred to an autoclave and sterilized in a laboratory steam autoclave. According to this description, the autoclaving (sterilization) is performed with the trial times and temperatures given in the following Table 4.

[0040] The analytical data of the carbohydrate components were obtained by high performance anion exchange chromatography (HPAEC) with NaOH as eluent and amperometric detection.

[0041] The germ and virus numbers obtained were substantially identical in all three trials. However, the isomaltulose decomposition was markedly reduced in the method according to the invention (Batches 2 and 3, 5 and 6) in contrast to the control batches with reduced temperature and longer sterilization time. A reduction of decomposition of about a 40% for the autoclaving step and of 22% for the overall process resulted from the shortening of the incubation times.

Table 4

Results:

			Batch 1	Batch 2	Batch 3
T	**(Temperature)**	**[°C]**	115	121	128
T	**(time)**	**[sec.]**	30	15	5
P	**(bar_{abs})**		1.7 (control)	2.1	2.5
Isomaltulose [g/kg]					
Solution before autoclaving			83.72	83.72	83.72
Solution after autoclaving			60.28	65.30	70.20
Isomaltulose during autoclaving [%]			28	22	16
Isomaltulose decomposition [%]			40	35	31